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(54) **Glass cartridge for injection syringe prefilled with pharmaceutical liquid**

Glassampulle für Injektionsspritze vorgefüllt mit flüssigem Arzneimittel

Cartouche en verre pour seringue d'injection pré-remplie d'un liquide pharmaceutique

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Description

FIELD OF THE INVENTION

[0001] The present invention relates to a glass cartridge applicable to an injection syringe having a capacity of 50 to 300ml prefilled with pharmaceutical liquid. In particular, the invention relates to a glass cartridge for an injection syringe capable of being prefilled with pharmaceutical liquid, wherein the glass cartridge comprises a barrel made of a heat-resistant glass tube such as a boro-silicate glass, etc., the barrel is closed by a lid provided on the exit end portion thereof, a tightly closed space defined by a stopper serving also as a piston which is positioned on the area of the inner part entrance thereof, is filled with pharmaceutical liquid beforehand, and a flange suited to a mechanism for loading it onto injecting device is provided on the entrance end portion.

BACKGROUND OF THE INVENTION

[0002] Currently, injection syringes are not supplied in the form that they are prefilled therein with pharmaceutical liquid scheduled to be used, when they are the ones having relatively large capacities of 50 to 300ml. Thus, under such circumstances, the system is always used, wherein after pharmaceutical liquid to be used are sucked into an empty syringe or an injection syringe (hereinafter called "an injection syringe") from a vial filled therewith via an injection needle, they are injected into a living body, such as a human body or the like.

[0003] The problem of this system lies in the fact that medical operators must do preparation work manually for replacing pharmaceutical liquid in the vial, and in particular it is necessary to repeat this work with the injection syringes having large capacities of 300ml by a number of times.

[0004] Also, a commonly used injection syringe made of plastics, such as a polypropylene etc., tends to get deformed due to a shortage of its own heat resistance and a rapid increase of an inner pressure when it is sterilized with steam water after being filled with liquid chemicals. Moreover, since a gas barrier characteristic of such a plastic syringe is poor, it has been impossible to use this type of the injection syringe for pharmaceutical liquid requiring a high level of a gas barrier characteristic. The plastic injection syringe also has a problem that, in order to prevent a deformation when carrying out sterilization with steam water, it requires a special technique comprising such as giving heat under increased pressure or cooling under decreased pressure.

[0005] In addition, a strong sliding resistance is gradually given to a rubber piston in the injection syringe made only of plastics, such as a polypropylene, etc., with the incursion of the rubber piston caused by a taper for withdrawal (smaller at end) of the syringe, the taper is almost unavoidably given to the inner wall of the plastics injection syringe. Thus, in the case where cartridges made of resins having capacities of 50 to 300ml, the cartridges are made impossible to be used as the sliding resistance reaches an unusual strength.

[0006] As it is known, for the object of preventing manual handling of the syringe or the injection syringe, an injection syringe made of glass having capacities of below 20ml has been produced, which comprises a barrel, an end wall sealing the exit end of the barrel and a liquid supplying hole provided for penetrating the end wall. However, in the case of glass cartridges having capacities of 50 to 300ml, residual stress caused by strong heat given for sealing or contracting the exit end tended to remain. This residual stress usually generated cracks on the exit end during transportation or storage. Further, such thermal stress also remained on a glass flange formed on the entrance end of the injection syringe, as well.

[0007] In the case where glass cartridges having relatively large capacities of 50 to 300ml tending to generate such thermal stress are produced from large diameter glass tubes, a sufficient annealing operation must be carried out so as to prevent cracks generated after formation and it leads to a steep reduction in productivity.

[0008] Further, as for large capacity injection syringes both of which ends are integrally processed from a large diameter glass tube directly, even when they are formed of neutral boro-silicate glasses, phase splitting is generated on glass components due to strong heat given to both ends. Consequently, during the process where liquid chemicals are poured into a formed injection syringe and sterilization by pressure steaming (for example, 121°C x 20 min) is operated in an autoclave, or during a long period of storage time thereafter, alkaline metal ions(Na+,K+,Ca++,B3+, etc.) from the inner surface of the glass barrel wall are eluted in pharmaceutical liquid, such pH of the pharmaceutical liquid shifts to an alkaline side on the average by 1 (See Table 1 as described later).

[0009] In result, pharmaceutical liquid easy to be affected by a change of pH usually get degraded in various ways. At the conventional system, as a means to prevent such degradation, a process for neutralizing alkali metal ions by a so-called "sulfur treatment", (treating with dil. H_2SO_4 solution) etc., has been required.

[0010] US-A-3941128 (Baldwin) discloses another prior art glass cartridge for an injection syringe.

OBJECT OF THE INVENTION

[0011] The present invention was made in order to provide a glass injection syringe which can be produced without causing residual stress on both ends of the glass tube body part. More specifically, the object of the present invention is to develop an injection syringe of easily sealing the exit end, easily attaching an injection needle, etc., and easily attaching its flange to the loading mechanism of an injection device at the entrance end, which can be produced, without an integral shaping which tends to cause residual stress and thus leads to a gross drop in productivity when such residual stress is eliminated.

SUMMARY OF THE INVENTION

[0012] The inventors intensely studied to solve the problems associated with the prior art and have found that cartridges to be used for the injection syringes having relatively large capacities of 50 to 300ml can be manufactured by using a glass tube without the integrate shaping.

[0013] That is, when only a barrel of a pharmaceutical liquid cartridge is formed of a glass tube such as a boro-silicate glass tube, the following effect was achieved:

- High-level heat resistance and gas barrier characteristic were realized;
- Prevention of alkalization of the inner surface generated due to phase splitting of the glass components and "sulfur treatment", etc., considered to be an essential post process can be made unnecessary.

[0014] A glass cartridge for an injection syringe prefilled with pharmaceutical liquid according to the present invention comprises a barrel of a heat resistant glass provided with an undercut on an outer surface of the exit end portion and another undercut on an outer surface of the entrance end portion reducing the diameter of the glass barrel, a lid holder made of a flexible material disposed on the exit end portion of the glass barrel to be engaged with the undercut, a gasket made of a soft material and disposed between the lid holder and the exit end of the glass barrel, a luer lock lid made of a flexible material provided between the gasket and the lid holder, a stopper serving also as a piston disposed in the glass barrel, and a flanged cap made of a flexible material provided on the entrance end portion of the glass barrel engaged with the undercut.

[0015] In the glass cartridge for the injection syringe of the present invention the glass barrel may be a linear transparent glass tube formed of a boro-silicate glass, provided with two or more pull-out preventive undercuts at the entrance end portion and exit end portion along a circumferential direction or adjacent two or more circumferential directions with holding a space therebetween, and the outer diameter of a portion of the flanged cap other than its flange is preferred to be not greater than those of the glass barrel.

[0016] In the glass cartridge for the injection syringe of the present invention, the luer lock lid can be an assembly made by laminating an inner luer lock lid and an outer luer lock lid, the inner luer lock lid in contact with the gasket is preferably formed of a polyolefin resin, the outer luer lock lid in contact with the lid holder is preferably formed of a resin selected from a thermoplastic polyester resin, a polyamide resin and a polysulfon resin; mixed resins of two or more of these; and mixed resins thereof with ethylene-vinyl alcohol copolymer.

[0017] In the glass cartridge for the injection syringe of the present invention, when the luer lock lid is the assembly made by combining an inner luer lock lid and an outer luer lock lid, the inner luer lock lid may comprise an outer cylindrical part having a collar on one end, which is disposed in the exit end portion of the glass barrel, a conical bottom part disposed on the other end of the barrel part and in inner cylinder starting from the vicinity of the central axis of the bottom part in a long and narrow tubular form, and an annular engaging projection line surrounding the base part of the inner cylinder, while the outer luer lock lid may be made to have a form roughly similar to that of the inner luer lock lid and be provided with an inner cylinder having an inner diameter large enough to be inserted thereinto the inner cylinder of the inner luer lock lid and an annular engaging projection on the entrance end of its inner cylinder which gets engaged with the annular engaging projection of the inner luer lock lid.

[0018] Further, on the glass cartridge for the injection syringe of the invention, both lid holder and flanged cap are preferably made of a polycarbonate resin.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] Fig. 1A shows a side view of a preferred embodiment of the glass cartridge for the injection syringe according to the present invention.

[0020] Fig. 1B shows a sectional view of the glass cartridge of the embodiment.

[0021] Fig. 2 shows an exploded sectional view of the glass cartridge of the embodiment.

EMBODIMENTS OF THE INVENTION

[0022] Preferred embodiments of the glass cartridge for the injection syringe according to the present invention will be described in detail with reference to the accompanying drawings.

[0023] Fig. 1A shows a side view of a preferred embodiment of the glass cartridge for the injection syringe according to the present invention, and Fig. 1B shows a sectional view thereof. As shown in Fig. 1A, in the glass cartridge of the embodiment, starting from a luer lock plug a connector and a pipeline connected to a catheter can be attached to the tip of the exit end side while a plunger can be attached from the entrance end. As shown in Fig. 1B, both the luer lock plug and the plunger can be detached while other members are maintained in an attached condition.

[0024] Fig. 2 shows an exploded longitudinal sectional view of the glass cartridge for the injection syringe of the embodiment.

[0025] As shown in Figs 1A, 1B and 2, the glass cartridge (1) of the embodiment comprises a barrel made of a glass tube (1a), a stopper (2) serving also as a piston provided inside the glass barrel (1a) beforehand, a gasket (3) attached so as to be brought into contact with the exit end (1e) and an inner surface of the glass barrel (1a) in the vicinity of the exit end (1e), a luer lock lid (4) attached to the exit end (1e) portion of the glass barrel (1a) via the gasket (3), a lid holder (5) fitted into the exit end (1e) portion of the glass barrel (1a) with holding the gasket (3) and the luer lock lid (4), and a flanged cap (6) provided on the entrance end (1i) portion of the glass barrel (1a).

[0026] Fig. 1B shows a plunger (7) to be fitted in the recessed part(2c) of the entrance side of the stopper (2) serving also as the piston.

<<GLASS BARREL 1a>>

[0027] The glass barrel (1a) is made of a transparent linear glass tube serving as an injection syringe main body. The glass barrel is provided with a pull-out preventive type undercut (1eu) on the outer surface of the exit end (1e) portion, the entrance end (1iu) portion which is a reduced diameter area (1iu) reduced in the diameter and extending from a large diameter part including the entrance end (1i) portion through a step-down part, and another pull-out preventive type undercut (1iu) on the outer surface of the entrance end (1i) portion. The size of the outer diameter of this entrance end portion (1ic) is reduced so as to allow the outer diameter of the flanged cap (6) provided thereon below that of other areas of the barrel (1a).

<<STOPPER (2) SERVING ALSO AS PISTON>>

[0028] The stopper (2) serving also as the piston comprises a head part (2h) having an obtuse apex angle toward its exit side and a body part (2b) roughly in a cylindrical form. The body part (2b) is provided with a recessed part (2c) on its entrance side surface (2i). The diameter and depth of the recessed part(2c) are large enough to house the head part(7h) of the plunger (7).

[0029] Three projection lines (2r) in circumferential direction are provided on the outer periphery of the stopper (2) serving also as the piston. They are commonly called rings and are brought into contact with the inner surface of the barrel (1a) to seal liquid being stuck to the inside of the glass cartridge (1). Thus, they (2r) are respectively independent of one another, the first is positioned on the skirt of the head part (2h), the second is positioned roughly on the middle of the body part (2b) and the third is positioned in the vicinity of the entrance end surface (2i) of the body part (2b).

<<GASKET (3)>>

[0030] The gasket(3) is disposed in the exit end (1e) portion of the glass barrel (1a) and comprises a main body (3f) of a ring form and an insertion part (3b) of a ring form projecting from an edge of an opening of the main body (3f) toward the glass barrel (1a). The main body (3f) of the gasket (3) is much thicker than the insertion part (3b). The main body (3f) is brought into contact with the exit end (1e) surface of the glass barrel (1a) while the insertion part (3b) is brought into contact with the inner surface of the exit end (1e) portion of the glass barrel (1a) to the inside slightly. The gasket (3) serves to tightly seal between the exit end (1e) surface of the glass barrel (1a) and the luer lock lid (4) which is brought into contact with the exit side (3e) surface of the gasket (3).

<<LURE LOCK LID (4)>>

[0031] The luer lock lid (4) is an assembly made by laminating an inner luer lock lid (41) and an outer luer lock lid (42). The inner luer lock lid (41) has a funnel-shaped bottom (41b) which makes the entrance side surface (41i) of the inner luer lock lid (41) have a recess roughly similar to the shape of the head part (2h) of the stopper (2) serving also as the piston so as to receive it. On the axis of the bottom 41 (b), the peripheral edge of a liquid supplying hole (41d)

is extended to form an inner cylinder (41cl) having the exit opening (41e). Further, on the periphery of the funnel-shaped bottom (41b) a pleated tube part (41s: outer cylinder) folded to the exit side and protruding roughly in parallel to the axis, and a flange part (41f) starting from the exit end of the pleated tube part (41s) are provided.

[0032] The exit side surface of the luer lock lid (41) has a shape having an apex angle formed similar to that of the entrance side surface. The shape of the exit side surface is also given by the connical bottom part (41b) having an obtuse angle, an outer cylinder (41s) steeply started from the end point of the bottom part (41b) and an inner cylinder (41t) starting from the center of the bottom within the inside of the outer cylinder (41s). The inner cylinder (41t) is made in a tapered and relatively thin cylindrical form. Further, an annular engaging projection (41m) surrounding the base part of the inner cylinder (41t) is provided.

[0033] On the other hand, the outer luer lock lid (42) is positioned on the outside of the inner luer lock lid (41), that is, in the same side of the lid holder (5) and made in a form roughly similar to the inner luer lock lid (41).

[0034] That is, the outer luer lock lid (42) comprises a conical funnel-shaped bottom (42b) with an obtuse apex angle, of which exit side (42e) surface is almost similar to the shape of the entrance side (42i) thereof and a cylindrical inner cylinder (42t) steeply starting from the center of the bottom part (42b). On the other hand, on the periphery of the bottom part (42b) the pleated tube (outer cylinder) part (42s) folded to the exit side and projected in parallel to the axis, and the flange part (42f) expanded from the tip of the plated tube part (42s) to the outside are provided.

[0035] The diameter of an inner cylinder (42t) of the outer luer lock lid (42) is formed relatively large and the inner cylinder (41t) of the inner luer lock lid (41) is inserted thereinto. On the inner surface of the one (42t) a means, for example, a male screw, for engaging with two slight projections (8a) and (8b) installed symmetrically on the lower end of the luer lock plug (8) is provided. Further, an annular engaging projection (42m) with a smaller diameter is provided on the inner base part of the inner cylinder (42t) of the outer luer lock lid (42) and engaged with the engaging annular projection (41m).

[0036] The back side of the flange part (42f) of the outer luer lock lid (42) is brought into contact with the surface of this flange part (41f) of the inner luer lock lid (41) and the outer luer lock lid (42) is housed without any loss in a space between the back side of the funnel-shaped part (41c) and the inner wall of the pleated tube part (41s) of the inner luer lock lid (41).

[0037] It should be noted that the bottom part (42b) and the pleated tube part (42s) of the outer luer lock lid (42) are housed without any loss in a space between the back side of the funnel-form part (41c) of the inner luer lock lid (41) and the inner wall of the pleated tube part (41s) folded from its periphery to the axial direction, and the flange part (42f) of the outer luer lock lid (42) is made smaller in the outer diameter than the flange part (41f) of the inner luer lock lid (41).

[0038] By such combination of the inner luer lock lid (41) and the outer luer lock lid (42) the inner luer lock lid (41) made from such as polyolefin (PO) comes into contact with a pharmaceutical liquid and leakage of the pharmaceutical liquid passed through between the gasket (3) and the inner luer lock lid (41) can be stopped by an outer luer lock lid (42) made from such as PBT.

<<LID HOLDER (5)>>

[0039] The lid holder (5) is a cylinder with a bottom, basically comprises a bottom plate (5b) and a cylindrical side wall (5w). The bottom Plate (5b) is provided with an opening (5m) having a diameter large enough to make the innder cylinder (42e) of the outer luer lock lid (42) project at the center of the bottom plate (5b). The lid holder (5) serves to hold and fix the luer lock lid (4) and the gasket (3) in the state that they are tightly stuck to the exit end (1e) of the glass barrel (1a).

[0040] The lid holder (5) is provided with an undercut (5ul) on the bottom plate side inner surface of its own side wall (5w) in order to restrain the luer lock lid (4) in the state that the inner cylinder (42t) of the outer luer lock lid (42) projects from the opening (5m) of its bottom plate (5b) up to the vicinity of its starting point and that the flange part (42f) of the outer luer lock lid (42) is in contact with the inner surface of the bottom plate (5b) of the lid holder (5).

[0041] The lid holder (5) is further provided with another undercut (5u2) on the entrance side inner surface within its side wall (5w) in order to fix both the flange parts (41f), (42f) of the luer lock lid (4) and the gasket (3) on the glass barrel (1a) with pressure. The section of this undercut (5u2) is roughly saw blade-shaped (unequal-sided projecting part), disposed for being engaged with the undercut (1eu) provided on the outer surface of the exit end (1e) portion of the glass barrel (1a), which allows to attach the lid holder (5) without any resistance but prevent its detachment.

[0042] Further, the sectional form of an undercut (5u1) positioned on the bottom side is also roughly saw blade-shaped, serving to prevent further advance of the one (1eu). Thus, it is preferred that its sectional triangle must be one having relatively equal sides and projecting rather high.

<<FLANGED CAP (6)>>

[0043] The flanged cap (6) is attached on the entrance end (1i) portion of the glass barrel (1a), including a flat flange

(6b) and a cylindrical tubular part (6p) starting from a face of the flange (6e) opposed to the entrance end (1i) of the glass barrel (1a). An opening (6m) is provided on the axis of the flange part (6b).

[0044] An undercut (6c) is provided on a predetermined position of the inner surface of the tubular part (6p) and engaged with the undercut (1eu) provided on the outer surface of the entrance end (1i) portion of the glass barrel (1a). The undercut (6c) is normally divided into two or more, in the case of the present embodiment it is divided into three or four. The value of a space between two adjacent undercuts (6c) is determined so as to make the undercuts(liu) of the glass barrel (1a) pass between the undercuts (6c) to be engaged therewith.

[0045] The undercut (1iu) may be also divided having the same number and the same sized space as the undercut (6c). However, the undercut (1iu) and/or the undercut (6c) may be successively and integrally formed. The shape of the undercut (6c) may be selected depending on the characteristics of a material of the flanged cap (6).

[0046] The sections of both undercuts are made in a saw blade-shape and designed such that they can prevent detachment of the flanged cap (6) but allow the cap (6) attached without any resistance. Further, the undercut (6c) is provided with a number of small ribs (6cr) protecting toward the inside from the inner surface of the flanged cap (6). A number of these small ribs are slightly deformed by the advance of the undercut (1iu), and serve to prevent rotation of the glass barrel (1s) by a slight pressure generated by the deformation and to limit its play.

[0047] The number of the small ribs (6cr) is preferably increased with the increase of the outer diameter of the entrance end (1ic) portion of the glass barrel (1a). In the case of the glass cartridge holding pharmaceutical liquid having a capacity of 50 - 300 ml the number must be normally from 10 to 16, preferably over 12, and they may be set at roughly equip-intervals among them. However, in the case where the undercuts (6c) present two or more, distance among small ribs means those among the ones existing on the same undercut (6c) but does not mean the spaces among the undercuts (6c).

[0048] The diameter of the opening (6m) is made roughly similar to the inner diameter of the entrance end (1i) of the glass barrel (1a). However, the inner diameter may be set at a value sufficient at least to allow the plunger (7) to be inserted therethrough.

<<ADDITIONAL MEMBERS>>

[0049] Additional members shown in Figs. 1A and 1B are not component parts of the glass cartridge (1) for the injection syringe prefilled with pharmaceutical liquid according to the present embodiment. However, they are members to be attached when the glass cartridge is put to actual use. These members will be described in brief.

<<PLUNGER (7)>>

[0050] Fig. 1B shows a glass cartridge (1) attached with the plunger (7) for use. The function is to advance the stopper (2) also serving as piston into the inside in the case where the glass cartridge (1) for the injection syringe prefilled with pharmaceutical liquid (1) is put to actual use.

[0051] As shown in Fig. 1B, the plunger (7) is constructed including a roughly conical main part (7g) and a head part (7h) of a short cylindrical part following the tip of the main part and usually has a roughly bar-shaped handle part (not shown) extending from the terminal end of the main part to the outside. The dimension and size of the head part (7h) is made suited to a recessed part (2c) provided on the bottom of the stopper (2) serving as piston. The plunger (7) serves to advance the stopper (2) serving as piston into the glass barrel (1a) in the state that the head part (7f) is fitted into the recessed part (2c) of the stopper (2).

[0052] A plunger of another embodiment (not shown) is used in the state that a plunger socket is integrally attached to its tip area. The form of the plunger in this case is roughly bar-shaped, and a male screw is provided on its tip area as means for engaging with a plunger socket which will be described below.

<<PLUNGER SOCKET (not shown) >>

[0053] Plunger socket is planned to be made separately from the above referred plunger of the another embodiment, but to be used by combining with it and made one unit.

[0054] In this case, the tip of the plunger is provided with a male screw for connecting the socket. The socket mainly constructs an insertion portion into the stopper (2) serving also as the piston and may have a flange in order to define its position integrally. Further, the socket has a female screw to be connected with the plunger main body.

<<LUER LOCK PLUG (8)>>

[0055] As shown in Figs. 1A and 1B, the luer lock plug (8a) is an opened conical tip part positioned on the luer lock lid side of a connector (an adapter) (8) connected to the catheter to be penetrated to an injection position. The luer

plug (8a) is provided with two slight projections (8b) symmetrically on a longitudinal axis on its tip. These projections (8b) are engaged with an engaging means, for example, a female screw provided on the inner cylinder (42t) of the outer luer lock lid (42) to fix the connector (8).

<<MATERIAL FOR EACH PART>>

[0056] Materials for respective component parts constructing the glass cartridge for the injection syringe filled with pharmaceutical liquid according to the present invention will be described.

[0057] The glass barrel (1) is desired to be made of a hard glass, preferably a heat resistant glass, more preferably a boro-silicate glass, in that it has a characteristic required by the present invention. Needless to say, it is most preferable that it is made of quartz in the view point of resistance to chemicals. Though boro-silicate glass is attacked to strong alkali, as strong alkaline chemicals are not usually used for medical purposes, no actual problem will occur. Further, it is much stronger than a hard glass in terms of resistance to thermal shock, etc.

[0058] The stopper serving also as (2) piston slidably fitted within the glass barrel (1a) and the gasket (3) attached to the exit end (1e) thereof are equally formed of soft materials, normally rubbers, and in particular a butyl rubber ("IIR", that is, isobutylene-isoprene copolymer rubber) is often used. These soft materials is desired to have an excellent gas barrier characteristic in addition to resistance to a heat of 121°C x 20 min (reduction in heat resistance, deformation by heat, etc., will not occur) which is a requirement for steam sterilization by pressure.

[0059] As for an assembly for forming the luer lock lid (4) to be fitted into the exit end (1e) of the glass barrel, the inner luer lock lid (41) and the outer luer lock lid (42) is made of flexible resins. In addition, the inner luer lock lid (41) is preferably formed of biochemically inert materials, such as a polyolefin (PO) resin including polypropylene resin and the outer luer lid (42) is preferably formed of materials having excellent heat resistance for preventing deformations and a good mechanical characteristic. For example, the materials for the outer luer lock lid (42) is selected from the group consisting of polybutylene terephthalate (PBT), polyamide (NY), polysulfon resins, mixed resins of two or more of these, and mixed resins of one or more of these with ethylene-vinyl alcohol copolymer (EVOH).

[0060] The lid holder (5) is lastly provided on the exit end (1e) of the glass barrel (1) so as to fix the luer lock lid (4) and the gasket (3) by pressure affixing them on the exit end (1e) thereof. Therefore, materials for the lid holder (5) is selected in view of a mechanical characteristic, heat resistance and mouldability rather than its interaction with contained chemicals. For example, a polycarbonate resin is often used, which is extremely excellent in view of exact dimensions of such as undercuts, etc., made by transferring from the shape of the metallic mold and the impact-proof properties.

[0061] Further, the flanged cap (6) is provided on the entrance end (1i) of the glass barrel (1a) and its flange (6b) serves as a fingerplate for pushing the the plunger (7) into the glass barrel (1a) and besides, it is important that it is suited to the loading device of the Auto-Injector normally on later use. Thus, a material for the flange (6) preferably has the same characteristic as the material for lid holder (5), and, therefore, a polycarbonate resin is commonly used.

[0062] The plunger (7) and the plunger socket are preferably all made of polyolefin resin, such as polypropylene resins. This selection has been made to be on the safe side, even though they are not brought into direct contact with pharmaceutical liquid. Of polypropylene resins, the one having resistance to pressurized steam sterilization is desired to be selected.

[0063] At the glass cartridge for the injection syringe prefilled with pharmaceutical liquid of the embodiment, the following effects are realized synergistically;

(a.) Engagements are made respectively between the pull-out preventive type undercuts (1iu) and (1eu) provided on the peripheries of the entrance and exit ends (1i), (1e) portions of the glass barrel (1u) and between the undercuts (6C) or (5C) projectingly and/or concavingly provided on the inner walls of the flanged cap (6) and the lid holder (5), and thereby liquid leakage and pull-out will be prevented when they are exposed to pressure steam sterilization (121°C x 20 min).

(b.) The luer lock lid (4) is assembled by combining the inner and outer luer lock lids (41), (42) and the former is made of a polyolefin resin, such as a polypropylene resin, while the latter is made of a resin material selected from high-melting point thermoplastic polyester such as PBT, thermoplastic polyamide such as 6-nylon, polysulfon resins, mixed resins of two or more of these, and the mixed resins of one or more of these with ethylene-vinyl alcohol copolymer resin(EVOH), and thus even when the resins lose their heat resistance due to pressurized steam sterilization (121°C x 20 min) and/or they are exposed to increase of inner pressure generated by e.g. expansion, evaporation, volatilization, etc. of pharmaceutical liquid, the condition that liquid leakage and pulling-out are prevented will be further strengthened.

(c.) The lid holder (5) and the flanged cap (6) are both made of a heat resistant thermoplastic resin, in particular a polycarbonate resin, and thus when they are exposed to steam sterilization by pressure (121°C x 20 min), liquid leakage and pulling-out will be effectively prevented. It practically suffices if the flange (6) is made of a polypropylene

resin.

(d.) Even when it is brought into contact with high-temperature pharmaceutical liquid during pressurized steam sterilization, alkaline metallic ions will not be eluted, and thus quality of pharmaceutical liquid will not be deteriorated.

EFFECT OF THE INVENTION

[0064] The following effects will be realized by using the glass cartridge for the injection syringe prefilled with pharmaceutical liquid according to the present invention:

(1) The cartridge made of general purpose, industrial material is not subject to liquid leakage and pull-out even when it is exposed to pressure steam sterilization (121°C x 20min).

(2) Even when it is brought into contact with high-temperature pharmaceutical liquid during pressurized steam sterilization, alkaline metallic ions will not be eluted, and thus quality of pharmaceutical liquid will not be deteriorated.

(3) It will be made possible to securely contain, transport and store a relatively large volume of pharmaceutical liquid ranging from 50 to 300ml, easily load it to the injection device as it is, and thereby to use for injecting pharmaceutical liquid.

(4) It will be made possible to use in the same manner as described above for medical use as X-ray Contrast Media, or the like difficult to be contained in the injection syringes.

(5) It will be made easy to break it down and divide it into combustibles and incombustibles prior to its disposing after use.

[0065] Hereinafter, the effects of the invention are concretely described in the following experiment.

EXPERIMENT

[0066] Glass syringes of the prior art each of which had integrally formed both ends, and syringes according to the present embodiment as shown in Fig. 1 having the same capacity were manufactured from various boro-silicate glasses. Into these syringes introduced was physiological saline (pH. 5.7) and they were subjected to pressurized steam sterilization (121°C x 1 h). Thereafter, the saline in each of syringes was measured in pH. The results are shown in Table 1.

[0067] As shown in Table 1, in each of syringes according to the embodiment of Fig. 1A, pH was hardly changed. From the results, it is understood that alkali components were difficult to elute into the saline.

Table 1

Variety of generally sold boro-silicate glasses		Elution index (pH) of alkaline components from the inner wall of the glass injection syringe		
Product name	Line expansion coefficient (x 10^{-7})	Sample No.	Products of this embodiments	Products with both ends (both end resin) integrally formed (both ends made of glass)
SIRIX	49	1	5.8	6.3
		2	5.7	6.2
		3	5.8	6.5
N-51-A	50	1	5.8	6.4
		2	5.8	6.5
		3	5.9	6.7
BS	52	1	5.9	6.8
		2	5.8	6.7
		3	5.9	6.9
Solvent for elution : Physiological salt solution (pH 5.7) Condition for sterilization (elution) by steaming under pressure: 121°C x 1 h				

Claims

1. A glass cartridge (1) for an injection syringe prefilled with pharmaceutical liquid, comprising a barrel (1a) of a heat resistant glass provided with an undercut (1eu) on an outer surface of the exit end portion (1e) a lid holder (5) made of a flexible material disposed on the exit end portion of the glass barrel to be engaged with the undercut (1eu), a gasket (3) made of a soft material and disposed between the lid holder and the exit end of the glass barrel and a stopper (2) serving also as a piston disposed in the glass barrel, **characterised in that** it further comprises a luer lock lid (4) made of a flexible material provided between the gasket and the lid holder, another undercut (1iu) on an outer surface of the entrance end portion (1i) reducing the diameter of the glass barrel, and a flanged cap (6) made of a flexible material provided on the entrance end portion of the glass barrel engaged with this undercut (1iu).

2. The glass cartridge for the injection syringe according to claim 1, wherein the glass barrel is a linear transparent glass tube formed of a boro-silicate glass, provided with two or more pull-out preventive undercuts at the entrance end portion and exit end portion along a circumferential direction or adjacent two or more circumferential directions with holding a space therebetween, and the outer diameter of a portion of the flanged cap other than its flange is preferred to be not greater than those of the glass barrel.

3. The glass cartridge for the injection syringe according to claim 1 or 2, wherein the luer lock lid is an assembly made by laminating an inner luer lock lid (41) and an outer luer lock lid, (42) the inner luer lock lid in contact with the gasket is formed of a polyolefin resin, the outer luer lock lid in contact with the lid holder is formed of a resin selected from a thermoplastic polyester resin, a polyamide resin and a polysulfon resin; mixed resins of two or more of these; and mixed resins thereof with ethylene-vinyl alcohol copolymer.

4. The glass cartridge for the injection syringe according to any of claims 1 to 3, when the luer lock lid is the assembly made by combining an inner luer lock lid and an outer luer lock lid, the inner luer lock lid comprise an outer cylindrical part (41s) having a collar on one end, which is disposed in the exit end portion of the glass barrel, a conical bottom part (41b) disposed on the other end of the barrel part and an inner cylinder (41t) starting from the vicinity of the central axis of the bottom part in a long and narrow tubular form, and an annular engaging projection (41m) line surrounding the base part of the inner cylinder, while the outer luer lock lid is made to have a form roughly similar to that of the inner luer lock lid and is provided with an inner cylinder (42t) having an inner diameter large enough to be inserted thereinto the inner cylinder of the inner luer lock lid and an annular engaging projection (42m) on the entrance end of its inner cylinder which gets engaged with the annular engaging projection of the inner luer lock lid.

5. The glass cartridge for the injection syringe according to any of claims 1 to 4, wherein both the lid holder and the flanged cap are formed of polycarbonate resins.

Patentansprüche

1. Glaspatrone (1) für eine Spritze, die mit pharmazeutischer Flüssigkeit vorgefüllt ist, umfassend einen Zylinder (la) aus einem wärmewiderstandsfähigen Glas, der auf einer Außenoberfläche des Ausgangsendbereichs (1e) mit einer Hinterschneidung (1eu) versehen ist, einen Deckelhalter (5), der aus flexiblem Material gefertigt ist, der auf dem Ausgangsendbereich des Glaszylinders angebracht ist, so dass er mit der Hinterschneidung (1eu) in Eingriff gebracht werden kann, eine Dichtung (3), die aus einem weichen Material gefertigt ist und zwischen dem Deckelhalter und dem Ausgangsende des Glaszylinders angebracht ist, und einen Anschlag (2), der auch als ein in dem Glaszylinder angebrachter Kolben dient, **dadurch gekennzeichnet, dass** sie ferner einen Luer-Arretierungsdekkel (4) der aus flexiblem Material gefertigt ist und zwischen der Dichtung und dem Deckelhalter vorgesehen ist, eine andere Hinterschneidung (liu) auf einer Außenoberfläche des Eingangsendbereichs (1i), der den Durchmesser des Glaszylinders kleiner werden lässt, und einen Deckel (6) mit Flansch umfasst, der aus einem flexiblen Material gefertigt ist, der auf dem Eingangsendbereich des Glaszylinders in Eingriff mit dieser Hinterschneidung (liu) vorgesehen ist.

2. Glaspatrone für die Spritze nach Anspruch 1, wobei der Glaszylinder ein gerades transparentes Glasrohr ist, das aus einem Borsilikatglas gefertigt, ist, der mit zwei oder mehr Hinterschneidungen, die das Herausziehen verhindern, am Eingangsendbereich und am Ausgangsendbereich entlang einer Umfangsrichtung oder mit zwei oder mehreren benachbarten Umfangsrichtungen versehen ist, wobei ein Abstand dazwischen eingehalten wird, und

wobei der Außendurchmesser eines Bereichs des Deckels mit Flansch ohne diesen Flansch vorzugsweise nicht größer als derjenige des Glaszylinders ist.

3. Glaspatrone für die Spritze nach Anspruch 1 oder 2, wobei der Luer-Arretierungsdeckel eine Anordnung ist, die durch Laminieren eines inneren Luer-Arretierungsdeckels (41) und eines äußeren Luer-Arretierungsdeckels (42) gefertigt ist, wobei der innere Luer-Arretierungsdeckel in Kontakt mit der Dichtung aus Polyolefinharz gefertigt ist, der äußere Luer-Arretierungsdeckel in Kontakt mit dem Deckelhalter aus einem Harz gefertigt ist, das ausgewählt wird aus einem thermoplastischen Polyesterharz, einem Polyamidharz und einem Polysulfonharz; gemischten Harzen aus zwei oder mehreren dieser Harze; und gemischten Harzen mit Ethylenvinylalkoholcopolymer.

4. Glaspatrone für die Spritze nach einem der Ansprüche 1 bis 3, wobei, wenn der Luer-Arretierungsdeckel eine Anordnung ist, die durch Kombinieren eines inneren Luer-Arretierungsdeckels und eines äußeren Luer-Arretierungsdeckels gefertigt ist, der innere Luer-Arretierungsdeckel einen äußeren zylindrischen Teil (41s), der an einem Ende einen Kragen aufweist, der in dem Ausgangsendbereich des Glaszylinders angeordnet ist, einen konischen Bodenteil (41b), der an dem anderen Endbereich des Zylinderteils angeordnet ist, und einen inneren Zylinder (41t), der in der Nähe der Mittelachse des Bodenteils in einer langen und engen röhrenförmigen Gestalt beginnt, und einen ringförmigen Eingriffslinienvorsprung (41m) umfasst, der den Bodenteil des inneren Zylinders umgibt, wobei der äußere Luer-Arretierungsdeckel in eine Gestalt gebracht ist, die im wesentlichen derjenigen des inneren Luer-Arretierungsdeckels ähnelt und mit einem inneren Zylinder (42t), der einen Innendurchmesser aufweist, der groß genug ist, in den inneren Zylinder des inneren Luer-Arretierungsdeckels eingeführt zu werden, und einem ringförmigen Eingriffsvorsprung (42m) am Eingangsende dieses inneren Zylinders versehen ist, der mit dem ringförmigen Eingriffsvorsprung des inneren Luer-Arretierungsdeckels in Eingriff kommt.

5. Glaspatrone für die Spritze nach einem der Ansprüche 1 bis 4, wobei sowohl der Deckelhalter als auch der Deckel mit Flansch aus Polycarbonatharzen gefertigt sind.

Revendications

1. Cartouche en verre (1) pour une seringue d'injection pré-remplie d'un liquide pharmaceutique, comprenant un barillet (la) réalisé en un verre résistant à la chaleur possédant un évidement (1eu) sur une surface externe de la partie d'extrémité de sortie (le), un support de couvercle (5) réalisé en un matériau souple disposé sur la partie d'extrémité de sortie du barillet en verre devant être engagé avec l'évidement (1eu), un joint d'étanchéité (3) réalisé en un matériau mou et disposé entre le support de couvercle et l'extrémité de sortie du barillet en verre, et une butée (2) servant aussi de piston disposée dans le barillet en verre, **caractérisé en ce qu'**elle comprend en outre :

   un couvercle de verrou de Luer (4) réalisé en un matériau souple prévu entre le joint d'étanchéité et le support de couvercle,
   un autre évidement (liu) sur une surface externe de la partie d'extrémité d'entrée (1i) réduisant le diamètre du barillet en verre,
   et un bouchon à rebords (6) réalisé en un matériau souple prévu sur la partie d'extrémité d'entrée du barillet en verre en prise avec cet évidemment (1iu).

2. Cartouche en verre pour la seringue d'injection selon la revendication 1, dans laquelle le barillet en verre est un tube droit en verre transparent formé à partir de verre borosilicaté, équipé de deux ou plusieurs évidements préventifs de traction au niveau de la partie d'extrémité d'entrée et de la partie d'extrémité de sortie le long d'une direction circonférentielle ou adjacents à deux ou plusieurs directions circonférentielles en maintenant un espace entre celles-ci, et le diamètre externe d'une partie du bouchon à rebords autre que son rebord n'est de préférence pas supérieur à celui du barillet en verre.

3. Cartouche en verre pour la seringue d'injection selon la revendication 1 ou 2, dans laquelle le couvercle de verrou de Luer est une structure réalisée en stratifiant un couvercle de verrou de Luer interne (41) et un couvercle de verrou de Luer externe (42), le couvercle de verrou de Luer interne en contact avec le joint d'étanchéité est formé en résine de polyoléfine, le couvercle de verrou de Luer externe en contact avec le support de couvercle est formé en une résine sélectionnée parmi une résine de polyester thermoplastique, une résine polyamide et une résine de polysulfone ; un mélange de deux ou de plusieurs de celles-ci ; et un mélange de ces résines avec un copolymère d'alcool de vinyléthylène.

4. Cartouche en verre pour la seringue d'injection selon l'une quelconque des revendications 1 à 3, dans laquelle le couvercle de verrou de Luer est la structure réalisée en combinant un couvercle de verrou de Luer interne et un couvercle de verrou de Luer externe, le couvercle de verrou de Luer interne comprend une partie cylindrique externe (41s) ayant un collier sur une extrémité, qui est disposée dans la partie d'extrémité de sortie du barillet en verre, une partie inférieure conique (41b) disposée sur l'autre extrémité de la partie du barillet et un cylindre interne (41t) partant de la proximité de l'axe central de la partie inférieure sous une forme tubulaire longue et étroite, et une ligne de projection d'engagement annulaire (41m) entourant la partie de base du cylindre interne, tandis que le couvercle de verrou de Luer externe est réalisé de façon à avoir une forme approximativement similaire à celle du couvercle de verrou de Luer interne et est équipé d'un cylindre interne (42t) ayant un diamètre interne suffisamment grand pour être inséré à l'intérieur du cylindre interne du couvercle de verrou de Luer interne et une saillie d'engagement annulaire (42m) sur l'extrémité d'entrée de son cylindre interne qui entre en prise avec la saillie d'engagement annulaire du couvercle de verrou de Luer interne.

5. Cartouche en verre pour la seringue d'injection selon l'une quelconque des revendications 1 à 4, dans laquelle à la fois le support de couvercle et le bouchon à rebords sont formés en des résines de polycarbonates.

Fig.1A

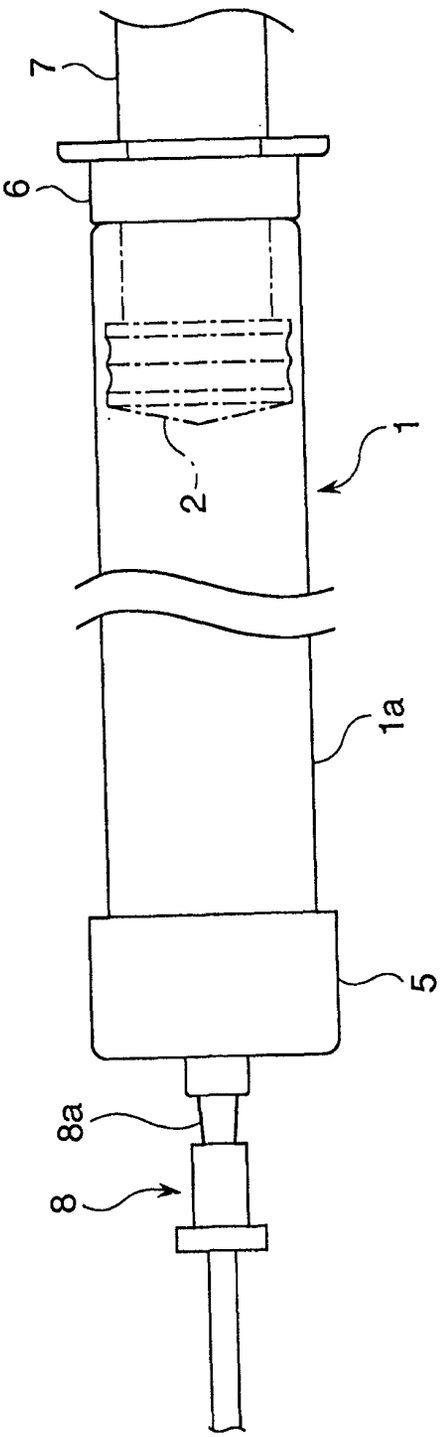

7
6
2
1
1a
5
8a
8

Fig.1B

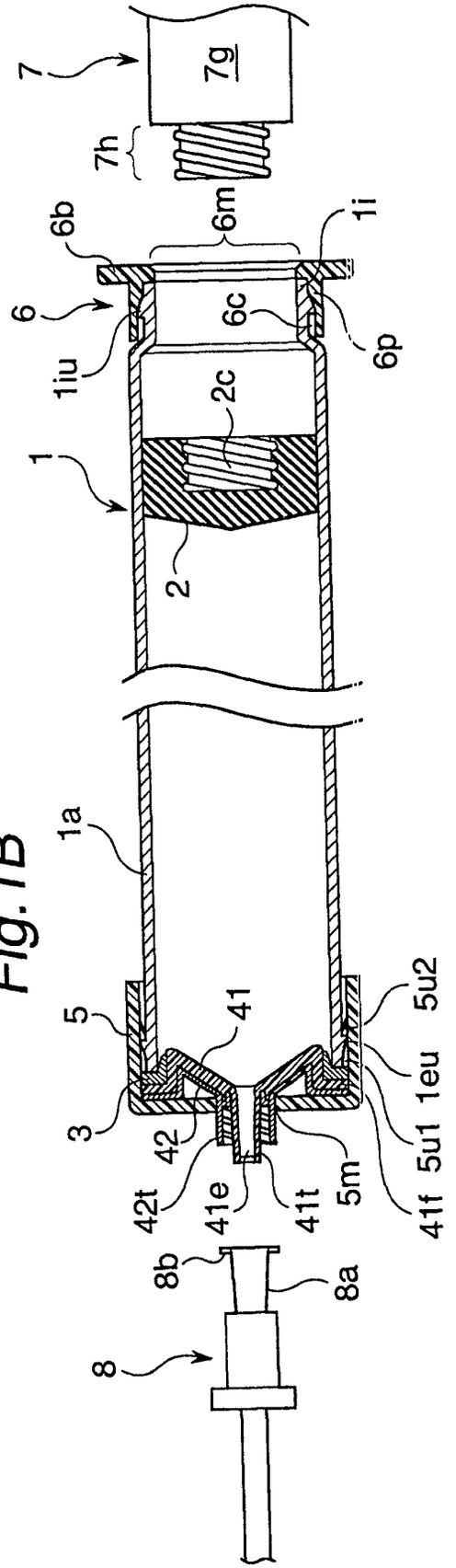
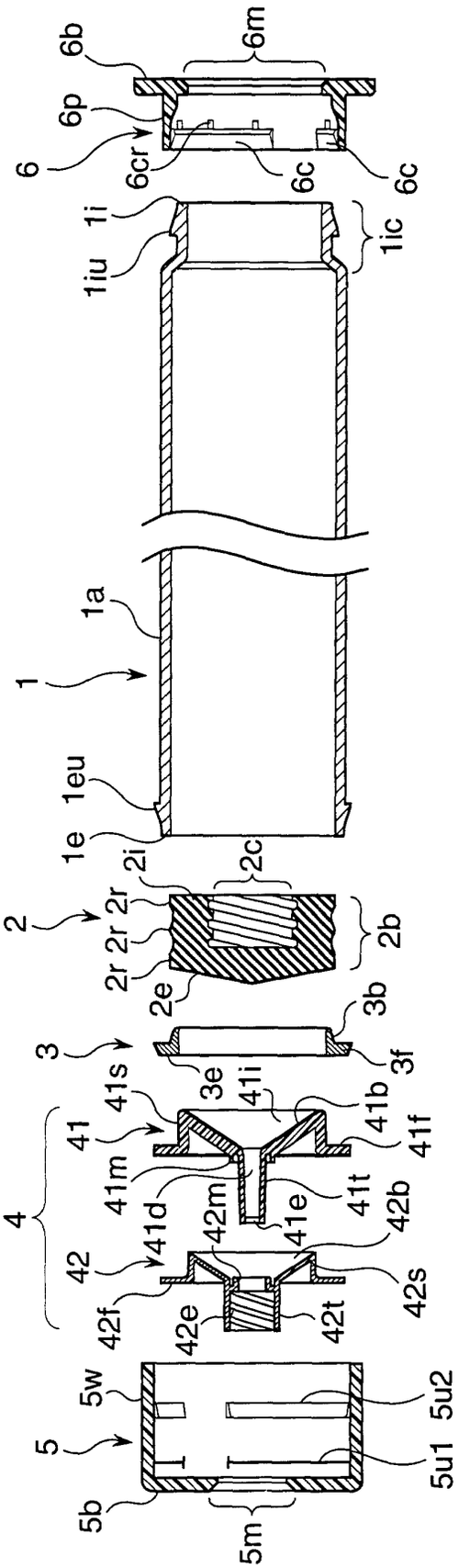

7
7g
7h
6b
6m
1i
6
6c
6p
1iu
2c
1
2
1a
5
41
5u2
3
42
1eu
5u1
42t
41e
41t
5m
41f
8b
8a
8

Fig.2


6b
6m
6p
6
6cr
6c
6c
1i
1ic
1iu
1
1a
1eu
1e
2i
2c
2
2r
2r
2r
2r
2b
2e
3b
3
3e
3f
41s
41i
41b
41
41f
41m
41d
42m
41e
41t
42b
4
42
42s
42f
42e
42t
5w
5u2
5
5u1
5b
5m